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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/811,028	03/25/2004	Michael Bennett	020714-002410US	9644

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EXAMINER	
KELLY, ROBERT M	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 03/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/811,028	BENNETT ET AL.	
	Examiner	Art Unit	
	Robert M. Kelly	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *24-33* is/are withdrawn from consideration.

5)☒ Claim(s) *34* is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 March 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *NOTICE TO COMPLY*.

DETAILED ACTION

Applicant's response to restriction requirement is entered.

Claims 1-34 are presently pending.

Election/Restrictions

Applicant's election with traverse of Group I, claims 2-23 and 34, and the species of (i) manganous superoxide dismutase, (ii) pMB-MnSOD, (iii) administration prior to irradiation of a salivary cell, in the reply filed on 12/23/05 is acknowledged. The traversal is on the ground(s) that Group I and IV should be rejoined, because they are classified in the same class, so it should not pose a serious burden to examine them together, and that the species elections are unduely limiting and they see no reason to limit it thusly.

This is not found persuasive because Groups I and IV, while classified in the same classification, such classification includes all gene therapy, with any vector, any disease, and any mechanism of action, and therefore the search and examination within such huge classification would necessarily not be coextensive, and the species elections are made for purposes of art rejection, and the purpose of such is to streamline prosecution. Applicant will still obtain a consideration of all species during the prosecution, therefore, Applicant's claims to unduely limiting are not persuasive, as in the end, Applicant is not being limited.

The requirement is still deemed proper and is therefore made FINAL.

Claims 24-33 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 12/23/05.

Claims 2-23 and 34 are presently considered with respect to the elected invention (methods of attenuating increases in radiation-induced free radicals or superoxide anions in a mammalian cell, and specific nucleic acids utilized in the methods).

Drawings

New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because drawing 2 is not clear, as to whether or not transcription of catalase is significant (i.e., the drawing does not appear to show bands, but a hand-drawn circle around the appropriate band location). Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Specification

The specification is objected to for containing sequences which require SEQ ID NO compliance.

Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Specifically the application fails to comply with CFR 1.821(d), which states:

(d) Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing " in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO: " in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

The specification discloses nucleotide and/or amino acid sequences page 27.

For compliance with sequence rules, it is necessary to include the sequence in the "Sequence Listing" and identify them with SEQ ID NO. In general, any sequence that is disclosed and/or claimed as a sequence, i.e., as a string of particular bases or amino acids, and that otherwise meets the criteria of 37 CFR 1.821(a), must be set forth in the "Sequence Listing." (see MPEP 2422.03).

For the response to this office action to be complete, Applicants are required to comply with the Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Claim Objections

Claims 2-6 are objected to because of the following informalities:

(i) Claim 2 recites "said one more proteins"; while it is clear that such claim is meant to claim "said one or more proteins", and hence, is not subject to a rejection under 112/2nd paragraph for lack of clarity, the claim requires proper use of English;

(ii) Claim 2 lists a Markush group of proteins, the first one beginning with the article "a", while the balance of the members do not have an article. Each member of the group requires a proper article, for proper English.

It is noted that Claims 3-6 depend from claim 2, and further exacerbate the incorrect English of Claim 2, and hence, such claims are also objected to.

Claim 23 is objected to because of the following informality:

Claim 23 recites "wherein said expression is sufficient ...". While it is clear Applicant is referring to the expression of the proteins encoded by the expression vector, and hence, the claim is not subject to a rejection under 112/2nd paragraph, proper English requires different terminology. For example, the Examiner suggests the terminology, "wherein the expression of the protein from the expression vector is sufficient ...".

Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 4, 8, 9-10, and 16 rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,599,712 by Greenberger.

With regard to claim 1-2, 4, and 8, Greenberger teaches protecting a cell from free radicals, superoxide anions, or heavy metal cations, by administration of a polynucleotide encoding a protein. Such protein is expressed and is capable of neutralizing or eliminating the various free radicals, superoxide anions, or heave metal cations that are elicited by the agent, and is particularly useful in protecting cancer patients against the damaging effects of ionizing radiation and chemotherapy. (ABSTRACT). Such protein is, e.g., manganous superoxide dismutase (cols. 6-7, paragraph bridging).

With regard to claim 9, Greenberger teaches treating humans (col. 7, paragraph 3).

With regard to Claim 10, Greenberger teaches administration prior to exposure to the agent/radiation (col. 2, paragraph 8).

With regard to Claim 16, because the gene is expressed, it is necessarily in an expression vector when delivered.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 20-21 rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,599,712 by Greenberger and Wagner, et al. (1990) Proc. Natl. Acad. Sci., USA, 87: 3410-14.

With regard to Claim 1, Greenberger teaches protecting a cell from free radicals, superoxide anions, or heavy metal cations, by administration of a polynucleotide encoding a protein. Such protein is expressed and is capable of neutralizing or eliminating the various free radicals, superoxide anions, or heave metal cations that are elicited by the agent, and is particularly useful in protecting cancer patients against the damaging effects of ionizing radiation and chemotherapy. (ABSTRACT). Such protein is, e.g., manganous superoxide dismutase (cols. 6-7, paragraph bridging).

However Greenberger does not teach administration of the nucleic acid with a polyionic organic acid, or with the further presence of a transition metal enhancer.

On the other hand, Wagner teaches that polylysine or protamine linked to transferrin, which transferrin contains an iron atom, can be used as a high-efficiency nucleic acid delivery system (ABSTRACT; p. 3411, col. 2, paragraph 2). Wagner teaches that all cells of the body contain this pathway of tranfection (p. 3410, paragraph 1) and further that the method avoids problems with cell death due to standard transfection protocols (p. 3414, col. 2, paragraph 2).

Hence, at the time of invention, it would have been obvious to modify the methods of Greenberger by using a plasmid and transferrin-infection as taught by Wagner. The Artisan would have been motivated to do so in order to transfect the cells in a highly efficient manner and avoid problems with cell death due to standard transfection protocols. Moreover, the Artisan would have had a reasonable expectation of success, as Wagner had shown that the mechanism is present in all actively metabolizing cells.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 9-10, 12, 18, and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,599,712 to Greenberger, and Jha, et al. (2000) Int. J. Radiation Oncology Biol. Phys., 46(1): 7-11.

Greenberger teaches protecting a cell from free radicals, superoxide anions, or heavy metal cations, by administration of a polynucleotide encoding a protein. Such protein is

expressed and is capable of neutralizing or eliminating the various free radicals, superoxide anions, or heave metal cations that are elicited by the agent, and is particularly useful in protecting cancer patients against the damaging effects of ionizing radiation and chemotherapy. (ABSTRACT). Such protein is, e.g., manganous superoxide dismutase (cols. 6-7, paragraph bridging). Moreover, such treatment is taught for humans (col. 7, paragraph 3) and the administration may be prior to exposure to the radiation (col. 2, paragraph 8), and further the administration may be directly to the cells requiring protection (e.g., col. 7, paragraph 3).

However, while Greenberger generally teaches any tissue requiring protection (e.g., col. 2, paragraph 4) and is for protecting such cells from the effects of ionizing radiation (e.g., col. 1, paragraph 3), Greenberger does not specifically teach treating salivary glands, to ameliorate symptoms of xerostomia.

On the other hand, Jha teaches that xerostomia is a significant form of morbidity in radiation therapy of the head and neck (ABSTRACT). Moreover, Jha teaches that removing the submandibular salivary gland prior to such treatments, then replacing the same gland, preserves its function and prevents the development of radiation-induced xerostomia (Id.). Hence, Jha teaches that the submandibular salivary gland is needed to be protected from ionizing radiation during treatment of head and neck cancers.

Hence, at the time of invention by Applicant, it would have been obvious to modify the methods of Greenberger and directly administer expression vectors encoding manganous superoxide dismutase directly to the submandibular salivary gland. The Artisan would have been motivated to do so to protect the patient from xerostomia due to ionizing radiation treatments because of head and neck cancers. Moreover, the Artisan would have had a

reasonable expectation of success, as Greenberger had taught the method of treatment to be successful, and Greenberger had shown the import of treating the submandibular salivary gland in such radiation treatments.

With regard to the composition, it is inherently obvious as it is made by the method.

With regard to this rejection, the rejection with respect to transition metal enhancers is made on the basis that Applicant's intended compositions comprising a transition metal are actually claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 1, 9-10, 12, 18, and 20-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,599,712 to Greenberger, and Jha, et al. (2000) Int. J. Radiation Oncology Biol. Phys., 46(1): 7-11 as applied to claims 1, 9-10, 12 above, and further in view of U.S. Patent Application Publication No. 2003/0198625 to Tseng, et al.

As shown above, Greenberger/Jha makes obvious Claims 1, 9-10, and 12, however they do not teach or suggest delivery intraductally, nor do they teach the use of polyionic organic acids or transition metal enhancers.

On the other hand, Tseng teaches enhanced transfection efficiency of the salivary gland through electroporation (ABSTRACT). Such nucleic acids may be delivered intraductally

(paragraph 0006) and the nucleic acid may be delivered with poly-L-glutamate and Zinc salts (paragraph 0009).

Hence, at the time of invention by Applicant, it would have been obvious to modify the methods of Greenberger/Jha with the intraductal administration and polyionic organic acid and Zinc salts of Tseng. The Artisan would have been motivated to do so in order to increase transfection efficiency. Moreover, the Artisan would have had a reasonable expectation of success, because Tseng teaches specifically transforming the submandibular glands (paragraph 0006).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejected claims encompass the generic limitation:

"a transition metal enhancer".

In order to understand what is encompassed by this limitations, and why they are claimed, the Aritsan looks first the to the specification.

With regard to transition metal enhancer, the definitions section of Applicant's specification states that transition metal enhancers are compounds having one or more transition metal atoms, which transition metals are actually broader than the classic transition metals of the periodic table, and include all transition metals, all lanthanides, all main-group metals (e.g., calcium), as long as the metals have similar properties to transition metal complexes (paragraph 0046). Aside from the broad language, such terminology indicates that any metal, and the Examiner also assumes, any of the lanthanides, that alone, and not in complexed in a compound, is encompassed, as long as these "metals" have a property similar to that of a compound that contains a transition metal complex. Such is simply very very broad, as any particular complex may have a property in common with another metal. E.g., they can be oxidized. Hence, the Artisan would look deeper into why such transition metal enhancers are part of the invention. The specification describes transition metal enhancers in more detail in paragraph 0086. However, such description simply indicates that that ionizable or ionized transition metals/metals may be used in treating xerostomia or xerophthalmia. The Artisan is similarly left to wonder what is this transition metal enhancer and why is it used in the invention?

The single reason given in the specification for such compounds is found in paragraph 0085, wherein Applicant states, "Surprisingly, the addition of a divalent metal to a formulation with suramin and DNA results in a synergistic increase in gene expression" (paragraph 0085). However, such divalent metal indicates that the transition metal enhancer must be a divalent metal, which is much more narrow in scope than the broad terminology used above. Moreover, the examples demonstrate only that Zinc Chloride and Suramin are present in the mixture with DNA when administered to rats.

However, such single demonstration of a single metal, zinc, does not mean that Applicant has possession of all transition metals, all lanthanides, and all metals with a property in common with any transition metal complexed compound, but only that Zinc Chloride, with Suramin, increases gene expression. Similarly, such demonstration of Suramin, in a composition with Zinc Chloride, does not demonstrate that all polyionic organic acids are possessed, or all antiviral compounds. Further with regard to the polyionic organic acid, the link between suramin and its antiviral activity appears to be completely unrelated to its increasing the expression of transfected transgene. Also, it is apparent that Applicant's claiming of such transition metal enhancers separate from the polyionic organic acid, as only the combination is disclosed to increase gene expression (paragraph 00085), and Applicant has provided no data in the specification to demonstrate that either alone could be used (e.g., EXAMPLES), and the examples do not even demonstrate that the combination increases gene expression, because all the examples that are not prophetic include such combination.

Next, having analyzed Applicant's disclosure, the Artisan would look to the art to understand why a polyionic organic acid may be administered with the nucleic acid, and further why any particular transition metal enhancer may be administered.

With regard to polyionic organic acids complexed with transition metals, it was well-known in the Art that polycationic nucleic acids could be used to increase transfection efficiency *in vivo*, e.g., Ramsay, et al. (2000) Int. J. Pharmaceutics, 210: 97-107 and Wagner, et al. (1990) Proc. Natl. Acad. Sci., USA., 87: 3410-14.

With regard to transition metals chelated in polyanionic organic acids, Tseng teaches that such divalent transition metals with polyanionic organic acids, wherein the transition metal is not

complexed to the acid, is also known for transformation of cells in electroporation techniques only (US 2003/0198625, paragraph 0093).

However, no Art of record demonstrates that any of Applicant's "transition metal enhancers" are possessed, beyond what is taught in the art, and Applicant single disclosure of suramin along with the transition metal Zinc, but such is not a complex, and hence is not a transition metal enhancer in the first place, because only the lanthanides and metals that are not transition metals, but have a common property are the members of the genera, are the members which may not be complexed as a compound (paragraph 0046).

Applicant's attention is directed to *In re Shokal*, 113 USPQ 283 (CCPA 1957), wherein it is stated:

> It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. *In re Soll*, 25 CCPA (Patents) 1309, 97 F2d 623, 38 USPQ 189; *In re Wahlforss*, 28 CCPA (Patents) 867, 117 F2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary.

Hence, beyond transferrin complexed to iron, and, if Applicant amends the claims accordingly, suramin in a composition with Zinc, Applicant is not in possession of generic species of a generic transition metal enhancer. (It is noted that the Zinc/Suramin is still not encompassed in the limitation because it is not complexed, but simply in a solution with suramin, e.g., EXAMPLE 1).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for direct or intra-ductal administration of vectors encoding proteins, operably linked to a promoter and polyA tail, to attenuate free radical and superoxide anion concentration increases in a cell due to ionizing radiation or alkalating agents, does not reasonably provide enablement for any other form of administration, the absence of promoter and poly A tail (i.e., non-expression vectors), or the administration of the nucleic acid after the cells are exposed to ionizing radiation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicant's claims encompass attenuating the increase in free radicals or superoxide anions in a cell, by administering a nucleic acid encoding a protein that is expressed and neutralizes/eliminates a portion of the free radicals or superoxide anions. Further dependent claims are drawn to the nucleic acid being an expression vector (Claim 16), and administration by intraductal or direct administration (Claims 18-19), and administration of the vector after exposure to ionizing radiation (Claim 11).

Clearly, if it is not an expression vector, the nucleic acid will not express the protein, and no treatment will be effected.

Further, these methods of administration may be by any method, and still reach the tissue type of interest to protect, and also, the administration of the vector after exposure of ionizing radiation is broad, as such administration may be well-after the damage has taken place.

To wit, it is generally recognized in gene therapy that enough cells must be transformed and express enough protein at the site of interest, and do so for a long enough period of time to effect treatment. For example, Vitolo, et al. (2002) Oral Diseases, 8 : 183-91, indicates that such transformation is reasonably predictable by intra-ductal or direct administration (e.g., p. 184, col. 1, paragraph 2), however, problems with administration occur such that many vectors are immediately cleared by the liver when delivered intravenously, and hence, would not even reach the intended glands, much less transform enough cells for a long enough period of time to effect treatment (e.g., McVie-Wylie, et al. (2003) J. Gene Med., 5: 399-406, ABSTRACT).

With regard to administration of the vector, if such vector was administered after the ionizing radiation, the free radicals would already have been present and acted to destroy the cells, and therefore, any damage would have been done, and subsequent expression of a transgene would have no effect in decreasing the increases.

Hence, Applicant's claims are only enabled for the scope given above.

Claims Free of the Art

Claim 34 is free of the art and allowable.

Conclusion

Claims 1-23 are rejected.

Claim 34 is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert M. Kelly, Art Unit 1633, whose telephone number is (571) 272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert M. Kelly, Ph.D.
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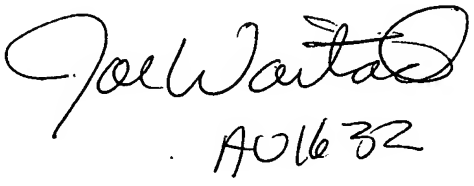

Application No.: 10/811,028

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: SEQUENCES IN SPECIFICATION NOT PROVIDED w/ SEQ ID NO and/or in Computer listing, or SEQUENCE LISTING

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
PatentIn Software Program Support
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